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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,247	01/15/2004	Raymond A. Dwek	2543-1-023CON	5331

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KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/758,247	DWEK ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006 and 18 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 12-42* is/are pending in the application.

4a) Of the above claim(s) *4-8,12,13 and 16-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 14, 15 and 39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Papers filed 21 September 2006 and 18 December 2006 in response to the Non-Final Office Action mailed 17 April 2006. Claims 4-8, 12, 13, and 16-38 were withdrawn from consideration and claims 1-3, 9-11, 14 and 15 were considered in the 17 April Office Action. Claims 2 and 9-11 were cancelled, claims 1 and 3 were amended and claims 39-42 were added in the 18 December Paper. Claims 1, 3-8 and 12-42 are pending and claims 1, 3, 14, 15 and 39-42 are under consideration.

Election/Restrictions

Newly amended claims 1, 3, 14, 15 and 39-42 are embrace an invention that is independent or distinct from the invention originally claimed for the following reasons:

As set forth in the Office Action mailed 2 February 2006, the methods practiced using an agent or bone marrow transplantation are distinct inventions. Applicant elected to prosecute the invention wherein an agent is coadministered in the Paper filed 2 February 2006. Although the amended claims recite, "[T]he agent capable of increasing the rate of glycolipid degradation is glucocerebrosidase or bone marrow transplantation." This recitation does not make sense in view of the fact that bone marrow transplantation is a process not "an agent". It is further noted that none of the teachings of "agent" in the disclosure as filed indicate that "bone marrow" is within the scope of "an agent" as used in the application.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, the claims will be examined as they read on the elected method wherein glucocerebrosidase is administered. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Amendment and Arguments

Rejection of claims 2 and 9-11 is rendered moot by the cancellation thereof.

Claim Rejections - 35 USC § 112

Rejection of claims 1, 3, 14 and 15 under 35 U.S.C. 112, first paragraph, as lacking adequate written description is **withdrawn** in view of the amendment of the claims such that the method is limited to practice with an imido sugar capable of inhibiting glucosylceramide synthase and a glucocerebrosidase enzyme.

Rejection of claims 1, 3, 14 and 15 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter is **withdrawn** in view of the amendment of the claims such that they no longer require prevention or cure of a glycolipid storage-related disorder and are limited to practice with an imido sugar capable of inhibiting glucosylceramide synthase and a glucocerebrosidase enzyme.

Rejection of claim 3 under 35 U.S.C. 112, second paragraph, is **withdrawn** in view of the amendment of the claim such that it depends directly from claim 1.

Double Patenting

Rejection of claims 1, 3, 14 and 15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 8 of U.S. Patent No. 6,696,059 is **withdrawn** in view of the filing of a terminal disclaimer.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 3, 14 and 15 under 35 U.S.C.§102(b) as being anticipated by Platt and Butters (1998; IDS AO) is **withdrawn**. In the paper filed 21 September 2006 (page 15, first full paragraph) Applicant argues persuasively that the Platt and Butters reference does not clearly teach that inhibitors of glucosylceramide synthase should be used in combination with glucocerebrosidase enzyme replacement.

Claims 1, 3, 14 and 15 **stand rejected** and newly added claims 39-42 **are rejected** under 35 U.S.C.§102(b) as being anticipated by Platt *et al.* (1998; IDS AF). This rejection is maintained for the reasons set forth in the previous Office Action at pages 14-17 and herein below in the response to Applicant's arguments. With respect to new claims 39-42, the claims differ from the previously rejected claims only in the outcomes recited in the claims. As the outcomes would be inherent to the methods of coadministering an imido sugar inhibitor of glucosylceramide synthase and glucocerebrosidase to a patient afflicted with a glycolipid storage-related disorder as taught in the prior art, absent evidence to the contrary, the claims are anticipated by the prior art for the reasons stated in rejecting claims 1, 3, 14 and 15.

Claims 1, 3, 14 and 15 **stand rejected** and newly added claims 39-42 **are rejected** under 35 U.S.C.§102(b) as being anticipated by Aerts et al. (1998; IDS AH). This rejection is maintained for the reasons set forth in the previous Office Action at pages 14-17 and herein below in the response to Applicant's arguments. With respect to new claims 39-42, the claims differ from the previously rejected claims only in the outcomes recited in the claims. As the outcomes would be inherent to the methods of coadministering an imido sugar inhibitor of glucosylceramide synthase and glucocerebrosidase to a patient afflicted with a glycolipid storage-related disorder as taught in the prior art, absent evidence to the contrary, the claims are anticipated by the prior art for the reasons stated in rejecting claims 1, 3, 14 and 15.

Response to Arguments

In response to the *prima facie* rejections of record, Applicant first contends that the invention is based on the surprising finding that NB-DNJ can act synergistically with either enzymes involved in glycolipid degradation or transplanted bone marrow and none of the prior art documents suggest this synergistic effect.

This argument has been fully considered but is not deemed persuasive because the claims are rejected under 35 U.S.C.§102 not 35 U.S.C.§103. Therefore, secondary considerations such as unexpected results and synergism are not relevant to the question of whether the art applies.

Next, Applicant points out that Platt et al. teaches that the N-butyl derivative of DNJ acts as an inhibitor of glucocerebrosidase in a cellular environment and contends that the authors did not appreciate that a combination of NB-DNJ and enzyme augmentation would be of any utility.

This argument is not deemed persuasive because the rejected claims are not limited to the use of NB-DNJ. Platt et al. explicitly teaches, "The N-alkyl DGJ may also be used in combination with glucocerebrosidase for the treatment of Gaucher disease." (column 3, lines 15-17) and that NB-DGJ does not inhibit the activity of glucocerebrosidase (column 10, final paragraph). Therefore, the claims are clearly anticipated by Platt et al. to the extent that they read on the method practiced with NB-DGJ.

With regard to Aerts et al. applicant contends that the disclosure of combination therapy therein is speculative and that Aerts et al. fails to enable the method. In particular, Applicant urges that Aerts et al. specifically teach away from the use of NB-DNJ in combination therapy in noting that NB-DNJ is known to inhibit lysosomal glucocerebrosidase.

This argument has been fully considered but is not deemed persuasive. The disclosure of Aerts et al. goes well beyond speculation. Although Aerts et al. does, as applicant points out, note that NB-DNJ is a known inhibitor of glucocerebrosidase, Aerts et al. demonstrates that butydeoxynojirimycin is a more than 1,000-fold more potent inhibitor of glucosylceramidase than glucocerebrosidase in *in vitro* experiments (see especially Table 3 and the caption thereto); and demonstrates that inhibition of glucosylceramidase can be achieved in intact cells using butyldeoxynojirimycin with no significant inhibition of glucocerebrosidase activity (see especially Table 4, Table 5 and the captions thereto). Thus, Aerts et al. demonstrates that agents such as NB-DNJ are sufficiently selective for glucosylceramidase over glucocerebrosidase that they can be used together. Given these teachings and the record as a whole, the skilled artisan would conclude that the disclosure of Aerts et al. is fully enabling for a method as claimed in the instant application.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand properly rejected under 35 U.S.C.§102(b) as anticipated by the art.

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 14, 15 and 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in reciting that the agent capable of increasing the rate of glycolipid degradation is bone marrow transplantation. As bone marrow transplantation is conventionally viewed as a process and there is nothing in the instant disclosure to indicate that bone marrow transplantation is redefined as a product, it is unclear what is intended by identifying bone marrow transplantation as within the scope of "an agent".

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Daniel M. Sullivan, Ph.D.
Primary Examiner
Art Unit 1636

DANIEL M. SULLIVAN, PH.D.
PRIMARY EXAMINER